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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JEFFREY OLSON, and VINCENT P. JR. STANTON

Appeal 2008-006230
Application 09/697,028
Technology Center 1600

Decided:[1] June 30, 2009

Before TONI R. SCHINER, DEMETRA J. MILLS, and LORA M. GREEN, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's final rejection of claims 10-16. We have jurisdiction under 35 U.S.C. § 6(b).

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

The claims are directed to a method for biasing a DNA amplification reaction at a polymorphic site. Claim 10 is representative of the claims on appeal, and reads as follows:

10. A method for biasing a DNA amplification reaction such that a first nucleic acid molecule having a first nucleotide present at a polymorphic site is amplified to a greater extent than a second nucleic acid having a second, different nucleotide present at the polymorphic site, comprising

(a) contacting a sample of DNA comprising at least the first nucleic acid molecule with two amplification primers that hybridize to both the first nucleic acid molecule and the second nucleic acid molecule at locations which flank the polymorphic site such that neither the first primer nor the second primer hybridizes to the polymorphic site, one of the two primers including a 5´ portion which, when incorporated into an amplification product, will upon further amplification yield products that form a stable stem-loop structure, the stem of which is perfectly matched and includes the polymorphic site only when the second nucleotide is present at the polymorphic site, but not when the first nucleotide is present at the polymorphic site; and

b) carrying out an amplification reaction, whereby the first nucleic acid molecule is amplified to a greater extent than the second nucleic acid molecule.

The Examiner relies on the following evidence:

Whitcombe	US 6,326,145 B1	Dec. 4, 2001

We reverse.

ISSUE

The Examiner finds that claims 10-16 are anticipated by Whitcombe.

Appellants contend that Whitcombe does not anticipate the claims on appeal as the probes described in the reference do not include a 5´ portion that is incorporated into an amplification product.

Thus, the issue on appeal is: Have Appellants demonstrated that the Examiner erred in finding that Whitcombe teaches the use of a primer including a 5´ portion which, when incorporated into an amplification product, will upon further amplification yield products that form a stable stem-loop structure, the stem of which is perfectly matched and includes the polymorphic site only when the second nucleotide is present at the polymorphic site, but not when the first nucleotide is present at the polymorphic site?

FINDINGS OF FACT

FF1 The claims on appeal "relate to DNA amplification methods that cause differential amplification of two nucleic acid molecules that differ in sequence at a polymorphic site." (App. Br. 2.)

FF2 According to the Specification:

> The method involves contacting a segment of DNA with two primers encompassing the polymorphic site under amplification conditions. One primer contains a region at its 5' end that is not complementary to the target nucleic acid but which, when incorporated into the amplification product, will cause the 3' end of the strand complementary to this primer in the amplification product to form a sufficiently stable hairpin loop by hybridizing with the sequence including the polymorphic site to inhibit further amplification only if the specific nucleotide is present at the polymorphic site. The method also involves determining whether the segment is amplified. Amplification (or preferential amplification) of the segment is indicative that the polymorphic site contains an alternative to the specific nucleotide.

(Spec. 10.)

FF3 The Examiner rejects claims 10-16 under 35 U.S.C. § 102(e) as being anticipated by Whitcombe (Ans. 2).

FF4 The Examiner finds that Whitcombe teaches a method of "biasing (enriching desired nucleic acid) a DNA amplification reaction such that a first nuclei [sic] acid having a first nucleotide present at a polymorphic site (allele 1) is amplified to a greater extent than a second nucleic acid having a second, different nucleotide present at the polymorphic site (allele 2)." (*Id.* at 3.)

FF5 The Examiner finds that Whitcombe teaches that "one of the two primers include[es] a 5´ portion which, when incorporated into an amplification product, will upon further amplification yield products that form a stable-stem-loop structure (see col. 7, line 49-67, col. 8, line 1-11, col. 9, line 2-24, indicate stem-loop structures when scorpion primers are used, Figs. 9, 11-12, indicating stem loop structures), the stem of which is perfectly matched and includes the polymorphic site only when the second nucleotide is present at [the] polymorphic site (allele-specific) (see col. 9, line 2-24, col. 10, line 53-67, col. 11, line 1-17, col. 13, line 45-52)." (*Id.*)

FF6 Whitcombe teaches "a tailed nucleic acid primer having a template binding region and [a] tail comprising a linker and target binding region." (Whitcombe, col. 1, l. 66-col. 2, l. 1.)

FF7 According to Whitcombe, the primer is used as an amplification primer in an amplification system, such as PCR, and the tail region is not copied, remaining single stranded (*id.* at col. 2, ll. 52-58).

FF8 The linker of the tailed nucleic acid primer thus may conveniently comprise a blocking moiety, such as a hexethylene glycol (HEG) monomer, which prevents polymerase mediated chain extension (*id.* at col. 2, ll. 61-64). Whitcombe also teaches the use of other blockers of polymerase mediated chain extension (col. 2, l. 64-col. 3, l. 5).

FF9 Whitcombe teaches that the sole requirement of the primer tail "is that the target binding region in the tail is available after primer extension to hybridise with a complementary sequence (if present) in the primer extension product." (*Id.* at col. 7, ll. 1-5.)

FF10 Whitcombe provides an Example wherein "a PCR was performed using primers which flank a polymorphism gene." (*Id.* at col. 13, ll. 16-19.) In the materials section, the Scorpion primers used contain a replication blocking hexethylene glycol monomer that is placed between the hairpin forming portion of the Scorpion primer (the tail region) and the portion used as the PCR primer (*id.* at col. 12, l. 51-col. 13, l. 3).

PRINCIPLES OF LAW

"It is well settled that a claim is anticipated if each and every limitation is found either expressly or inherently in a single prior art reference." *Celeritas Techs. Ltd. v. Rockwell Int'l Corp.*, 150 F.3d 1354, 1361 (Fed. Cir. 1998).

ANALYSIS

Appellants contend that Whitcombe cannot anticipate the claims on appeal as "the probes described [by Whitcombe] do not include a 5´ portion

that is incorporated into an amplification product." (App. Br. 5.) According to Appellants, Whitcombe teaches that it is the 5´ end of the Scorpion probe that forms the stem-loop structure, and Whitcombe teaches that the 5´ end of the Scorpion probe is not amplified (*id.* at 7). Appellants therefore assert "the Scorpion probes do not contain a 5´ region that is incorporated into the amplification product and forms a stem-loop structure (when a certain target sequence is present), as required by the present claims." (*Id.*)

The Examiner responds that "Appellants' arguments are based solely on the detection probes of [Whitcombe] and are silent with regard to the Scorpion primers, which are involved in the amplification process." (Ans. 8.) As noted by Whitcombe, however, the primary purpose of the tail region, which is not amplified and thus remains single stranded, is that the target binding region of the tail is available after primer extension to hybridize with a complementary sequence (if present) in the primer extension product. Thus, the stem-loop structure of Whitcombe is formed by the tail region of the Scorpion primer of Whitcombe, which is specifically blocked from being incorporated into the amplification product, whereas the independent claims on appeal (claims 10 and 16) require that one of the two primers includes a 5´ portion which, *when incorporated into an amplification product*, will upon further amplification yield products that form a stable stem-loop structure.

CONCLUSION(S) OF LAW

We therefore find that Appellants have demonstrated that the Examiner erred in finding that Whitcombe teaches the use of a primer

including a 5´ portion which, when incorporated into an amplification product, will upon further amplification yield products that form a stable stem-loop structure, the stem of which is perfectly matched and includes the polymorphic site only when the second nucleotide is present at the polymorphic site, but not when the first nucleotide is present at the polymorphic site.

The rejection of claims 10-16 under 35 U.S.C. § 102(e) as being anticipated by Whitcombe is thus reversed.

REVERSED

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